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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/308,295	05/17/1999	ABBOT F. CLARK	1581US	5973

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EXAMINER
BASI, NIRMAL SINGH

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/10/2002 17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/308,295	Applicant(s) Clark Etal
	Examiner Nirmal S. Basi	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Jun 19, 2002* .

2a) [ ] This action is **FINAL**. 2b) [X] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *1, 2, and 5* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *1, 2, and 5* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are a) [ ] accepted or b) [ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____ .
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) [ ] The translation of the foreign language provisional application has been received.

15) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [ ] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) [ ] Interview Summary (PTO-413) Paper No(s). _____
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other: _____

DETAILED ACTION

1. The request filed on 6/19/02 (paper number 15) for a Continued Examination (RCE) under 37 CFR 1.144 is accepted and a RCE has been established. An action on the RCE follows:

2. Amendment filed 6/19/02 (paper number 16) has been entered.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action (7/30/01, paper number 8).

Claim Rejection, 35 U.S.C. 112

4. Claims 1, 2 and 5 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record in the office action of 10/13/01, paper number 4 .

Claim 1 is indefinite because it is not clear how the biological sample is analyzed for the expression of SEQ ID NO:2 so as to allow the metes and bounds of the claim to be determined. . Further, SEQ ID NO:2 is a sequence of amino acids, which by itself can not be expressed, the protein corresponding to the amino acid sequence of SEQ ID NO:2 is expressed. Therefore the analysis of SEQ ID NO:2 is indefinite. It is suggested the claim be amended to include the "protein corresponding to SEQ ID NO:2" to overcome the rejection. Also it is not clear what is aberrant expression of SEQ ID NO:2 or a defect in a GR gene encoding SEQ ID NO:1. Similarly SEQ ID NO:1 and 2 are mere characters and should be amended to include nucleic acid of SEQ

ID NO:1 and protein of SEQ ID NO:2. Also it is not clear what is aberrant expression of SEQ ID NO:2 so as to allow the metes and bounds of the claim to be determined. For example does aberrant expression imply quantity or homology? Also aberrant can only be determined by comparing to a control, there is no comparison to a control in the claim. Also it is not clear how the defect in the GR gene is determined by comparison to SEQ ID NO:1 since no gene is disclosed, SEQ ID NO:1 is RNA. Also it is not clear how the defect in GR gene encoding SEQ ID NO:2 as compared to SEQ ID NO:1 indicate a diagnosis of glaucoma since the method does not include a step to determine a gene defect.

Claim 2 remains rejected due to the improper Markush grouping. The claim refers to a group containing both methods and non-methods. Applicant argues, "Claim 2 is directed to a listing of assays of DNA analysis that can be used to detect GRβ expression. These assays or methods; including denaturing gradient gel are specifically set forth in the" Applicants arguments have been fully considered but not found persuasive. Denaturing gradient gel and single-stranded conformation polymorphism (SSCP) are not methods. For example, denaturing gradient gel is a type of gel and not a method. Denaturing gradient gel electrophoresis is a method. Further there is a lack of antecedent basis for the use of detection "gene defect" in claim 2. Claim 1, on which claim 2 depends, does not contain a step for detecting gene defects. Claim 1 only has a step for detecting expression of the SEQ ID NO:2, which is not a gene. Further it is not clear how each of the methods in claim 2 specifically detect gene defects. For example what primers are used, how is allele specific hybridization determined since no allele is disclosed etc.

Claim 5 is indefinite because it is not clear how the method determines if an agent can alter the expression of SEQ ID NO:2 if the method is practiced in the absence of proteins and nucleotides required for expression. The method is not limited to use of whole cells or cell extracts. Further is not clear if increase in expression of SEQ ID NO:2 determines if an agent is useful for treating glaucoma or decrease in expression determines if an agent is useful for threatening glaucoma. Also it is not clear what is meant by interacts so as to allow the metes and bounds of the claims to be determined. For example water interacts with all proteins in some way. The claims are also indefinite for use of SEQ ID NO:s without indicating whether they are nucleic acid of protein for reasons given above.

Claim Rejection, 35 U.S.C. 112

5. Claims 1, 2 and 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling a method for diagnosing glaucoma in a person comprising obtaining a biological sample from trabecular meshwork of said person and analyzing the sample for the presence for expression of the protein of SEQ ID NO:2 wherein the expression of the protein of SEQ ID NO:2 indicates a positive diagnosis of glaucoma, does not reasonably provide enablement for other methods. The, specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1 and 2 are drawn to a method of diagnosing glaucoma which comprises detecting aberrant expression of SEQ ID NO:2 or defect in the gene encoding SEQ ID NO:2. Claim 5 is drawn to method of determining whether an agent is useful for treating glaucoma by determining whether the agent interacts with SEQ ID NO:1 or alters expression of SEQ ID NO:2. The specification and applicants arguments disclose that the trabecular meshwork (TM) of glaucoma patients express both GRbeta and Gralpha whereas the TM of non-glaucomous patients expresses only GRalpha. Therefore the conclusion is made that the presence of GRbeta in TN of a patient reveals the presence of glaucoma.

The claims encompass the aberrant expression of the protein of SEQ ID NO:2 as a diagnosis of glaucoma or a defect in the gene encoding the protein of SEQ ID NO:2 as compared to the nucleic acid of SEQ ID NO:1 as indicating a diagnosis of glaucoma. The term aberrant expression encompasses, for example, different levels of expression as well as expression of different isoforms off the protein. The specification discloses that the presence of GR beta is indicative of glaucoma, not aberrant expression used in its full scope. Further no gene encoding GR is disclosed, SEQ ID NO:1 is RNA. Therefore it is not clear what defect in the GR gene is indicative of glaucoma. Claim 5 encompasses interacting an agent with the nucleic acid represented by SEQ ID NO:1 or protein SEQ ID NO:2 and determining if the agent interacts with the nucleic acid or alters expression of the protein. There is no limitation that whether an increase or decrease in interaction or expression determines if the agent is useful for treating glaucoma. There is no disclosure in the specification to provide support that an gent that

interacts with nucleic acid represented by SEQ ID NO:1 will have any effect. For example water interacts with nucleic acid of SEQ ID NO:1, but does not have an effect on treating glaucoma in instant method. Further there is no indication that altering expression will treat glaucoma. On the contrary increased expression of the protein of SEQ ID NO:2 will have an adverse effect. All agents that interact with nucleic acid represented by SEQ ID NO:1 or alter expression of the protein of SEQ ID NO:2 will not necessarily treat glaucoma. Further, the claims suggest possible general assays which may be used to achieve the goal of the preamble but the specification, claims or prior art do not state how to use said assays to specifically diagnose glaucoma. Also there is no disclosure that expression of GR beta in other tissues, apart from TM, is indicative of glaucoma. Therefore, without evidence that detection of GRbeta in all tissue is indicative of a diagnosis for glaucoma, and the defects required to determine the diagnosis of glaucoma, lack of assay steps in the method claims, the complex nature of the interactions in the disease state of glaucoma and the unpredictability of determining if agents that interact with nucleic acid of SEQ ID NO:1 or alter expression of the protein of SEQ ID NO:2 will be useful for treating glaucoma does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope of claims 1, 2 and 5.

Claim 1 and 5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Following the preamble in claim 1 the method recites the steps of :

(a) obtaining a biological sample from said person; and

(b) analyzing said sample for expression of SEQ ID NO:;

wherein aberrant expression of SEQ ID NO: or a defect in a GR gene encoding SEQ ID NO:2 as compared to SEQ ID NO:1 indicates a diagnosis of glaucoma.

Following the preamble in claim 5 the method recites:

(a)obtaining a composition comprising SEQ ID NO:1 or SEQ ID NO:2;

(b)admixing said composition with an agent; and

determining whether the agent interacts with SEQ ID NO:1 or alters the expression of SEQ ID NO:2.

The claiming of SEQ ID NO:1 and SEQ ID NO:2, the steps (a) and (b) in both claims 1 and 5, as well as the final determining steps are a new concept not appearing in the originally filed application. Applicant argues no new matter is added and that material incorporated by reference may be added into the specification. Applicants arguments have been fully considered but not found persuasive. The specification does not include any referees "incorporated by reference". Further SEQ ID NO:1 and SEQ ID NO:2 are not included in the specification and cannot be incorporated by reference since literature containing said sequence is not contained in the

specification and also not "incorporated by reference". If Applicant feels this rejection is in error then Applicant must provide specific support in the specification for the amendments to claims 1 and 5, as well as to where in the specification, the references Applicant considers relevant, are specifically "incorporated by reference".

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
September 9, 2002

Michael D. Pak
MICHAEL PAK
PRIMARY EXAMINER